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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Kurt Nilsson, et al		
Appln. No.	:	Unassigned	Group Art Unit:	Unassigned
Filed	:	January 23, 2001	Examiner:	Unassigned
For	:	IMMOBILIZED CARBOHYDRATE BIOSENSOR		

PRELIMINARY AMENDMENT

Assistant Commissioner of Patents
Washington, D.C. 20231

January 23, 2001

Dear Sir:

Prior to examination on the merits in this continuation application, please amend the above-identified patent application as follows:

IN THE SPECIFICATION:

In the line following the title, please insert:

--This is a continuation application based on U.S. Pat. Appln. No. 08/356,229, filed December 12, 1994; which in turn is a continuation application of PCT/SE94/00343, filed April 18, 1994; which was in turn based on Swedish Priority Document 9301270-6, filed April 19, 1993. All of these documents are relied upon and incorporated by reference herein, in their entirety.--

IN THE CLAIMS:

Please cancel claims 1-16 from the application.

Please add new claims 17-69 as follows:

--17. An immobilized carbohydrate derivative biosensor, comprising:

a surface; and

a carbohydrate derivative, bound to the surface, which specifically binds to at least one biomolecule in a sample.

18. The immobilized carbohydrate derivative biosensor according to claim 17, wherein the carbohydrate derivative comprises a fragment of a carbohydrate sequence found in a glycoprotein or a glycolipid.

19. The immobilized carbohydrate derivative biosensor according to claim 18, wherein the fragment of a carbohydrate sequence found in a glycoprotein or a glycolipid comprises an oligosaccharide.

20. The immobilized carbohydrate derivative biosensor according to claim 19, wherein the oligosaccharide comprises a smaller fragment selected from the group consisting of a disaccharide, a trisaccharide, a tetrasaccharide and a pentasaccharide.

21. The immobilized carbohydrate derivative biosensor according to claim 20, wherein the smaller fragment is of a size sufficient for the oligosaccharide to bind the at least one biomolecule.

22. The immobilized carbohydrate derivative biosensor according to claim 19, wherein the oligosaccharide is modified in the reducing end with an aglycon comprising a glycosidically bound organic group by which the oligosaccharide is bound to the surface of the biosensor.

23. The immobilized carbohydrate derivative biosensor according to claim 22, wherein the aglycon is a member selected from the group consisting of -OEtSEtCONHNH$_2$ and -OEtSPhNH$_2$.

24. The immobilized carbohydrate derivative biosensor according to claim 17, wherein the carbohydrate derivative is directly bound to the surface.

25. The immobilized carbohydrate derivative biosensor according to claim 17, wherein the carbohydrate derivative is bound to the surface via a protein.

26. The immobilized carbohydrate derivative biosensor according to claim 25, wherein the protein comprises bovine serum albumin.

27. The immobilized carbohydrate derivative biosensor according to claim 17, wherein the carbohydrate derivative is bound to the surface via a chemical structure which has been adsorbed.

28. The immobilized carbohydrate derivative biosensor according to claim 17, wherein the carbohydrate derivative is bound to the surface via a chemical structure which has been covalently bound to the surface.

29. The immobilized carbohydrate derivative biosensor according to claim 22, wherein the carbohydrate derivative is bound to the surface via a chemical structure which has been covalently bound to the surface.

30. The immobilized carbohydrate derivative biosensor according to claim 29, wherein the chemical structure which has been covalently bound to the surface contains a reactive organic group selected from the group consisting of a carboxyl, a sulfonate, a cyanate, an epoxy and an aldehyde group which chemically conjugates with an amine or thiol group of the aglycon.

31. The immobilized carbohydrate derivative biosensor according to claim 17, wherein the biomolecule is at least one member selected from the group consisting of a protein, a virus and a cell.

32. The immobilized carbohydrate derivative biosensor according to claim 17, wherein the biomolecule is at least one member selected from the group consisting of a lectin, an antibody against a carbohydrate, a pathogenic virus, a pathogenic bacteria, a saccharide, a peptide and a protein.

33. The immobilized carbohydrate derivative biosensor according to claim 17, wherein the carbohydrate derivative is selected from the group consisting of a blood group determinant; a cancer-associated carbohydrate sequence; a carbohydrate sequence which binds to a pathogenic bacteria, a pathogenic toxin or a virus; and a carbohydrate sequence which binds to a protein, a cell, or a white blood cell associated with an inflammatory reaction.

34. The immobilized carbohydrate derivative biosensor according to claim 17, wherein the carbohydrate derivative contains at least one of the following monosaccharides: hexosamine, fucose, mannose, glucose, N-acetyl-glucosamine, N-acetyl-galactosamine, xylose and galactose.

35. The immobilized carbohydrate derivative biosensor according to claim 17, wherein the at least one monosaccharide is present in pyranose or furanose form.

36. The immobilized carbohydrate derivative biosensor according to claim 17, wherein the carbohydrate derivative is a derivative in which the carbohydrate is modified in the reducing end with an O-, N-, C- or S-glycosidically bound aglycon.

37. The immobilized carbohydrate derivative biosensor according to claim 36, wherein the glycosidically bound aglycon is a member selected from an aliphatic compound, an aromatic compound, an amino acid molecule, a peptide molecule and a protein molecule.

38. The immobilized carbohydrate derivative biosensor according to claim 17, wherein the carbohydrate derivative is a carbohydrate in which one or more of the hydroxyl groups, in addition to or instead of the hydroxyl group in the reducing end of the carbohydrate part, is modified with an organic group or an inorganic group.

39. The immobilized carbohydrate derivative biosensor according to claim 36, wherein the aglycon is adsorbed or covalently bound to the surface of the biosensor and serves as a spacer molecule between the biosensor surface and the carbohydrate derivative to minimize sterical hindrance in the binding of the biomolecule to the carbohydrate derivative.

40. The immobilized carbohydrate derivative biosensor according to claim 36, wherein the glycosidically bound aglycon comprises a structure corresponding to a formula -R-X.

41. The immobilized carbohydrate derivative biosensor according to claim 40, wherein R comprises an organic compound, and wherein -X is a member selected from the group consisting of -S-, -NH-CO-, CO-NH-, -NH-, and -N=N-.

42. The immobilized carbohydrate derivative biosensor according to claim 40, wherein R comprises a member selected from the group consisting of: an alkyl chain of the formula $(-CH_2)_n$, in which n is an integer from 2 to 8; and an aromatic group.

43. The immobilized carbohydrate derivative biosensor according to claim 40, wherein the carbohydrate derivative comprises a neoglycoprotein, and wherein the structure corresponding to the formula -R-X comprises a spacer between a protein part and a carbohydrate part of the neoglycoprotein, and wherein -X binds to the protein part of the neoglycoprotein.

44. The immobilized carbohydrate derivative biosensor according to claim 17, wherein the carbohydrate derivative comprises a member selected from the group consisting of an isolated glycoprotein, a recombinant glycoprotein and a glycopeptide.

45. The immobilized carbohydrate derivative biosensor according to claim 17, wherein the surface comprises a member selected from the group consisting of a gold surface and a silica surface.

46. The immobilized carbohydrate derivative biosensor according to claim 17, wherein the surface adsorbs at least one member selected from the group consisting of a protein, a lipid and a peptide.

47. The immobilized carbohydrate derivative biosensor according to claim 17, wherein the carbohydrate derivative is a neoglycoprotein, and wherein a protein part of the neoglycoprotein comprises a member selected from the group consisting of an amino group, a carboxyl group and a thiol group, which member is bound to the surface of the biosensor.

48. The immobilized carbohydrate derivative biosensor according to claim 40, wherein the biosensor corresponds to the formula carbohydrate-R-X-biosensor surface.

49. The immobilized carbohydrate derivative biosensor according to claim 40, wherein the biosensor corresponds to the formula carbohydrate-R-X-protein-biosensor surface.

50. The immobilized carbohydrate derivative biosensor according to claim 49, wherein the X portion and the protein are directly adsorbed on the biosensor surface.

51. The immobilized carbohydrate derivative biosensor according to claim 40, wherein the biosensor corresponds to the formula carbohydrate-R-NH-CO-CH_2-CH_2-S-biosensor surface.

52. The immobilized carbohydrate derivative biosensor according to claim 49, wherein the biosensor corresponds to the formula carbohydrate-R-X-protein-NH-CO-CH_2-CH_2-S-biosensor surface.

53. The immobilized carbohydrate derivative biosensor according to claim 49, wherein the protein comprises bovine serum albumin.

54. The immobilized carbohydrate derivative biosensor according to claim 52, wherein the protein comprises bovine serum albumin.

55. The immobilized carbohydrate derivative biosensor according to claim 17, wherein a configuration of the biosensor is a configuration selected from the group consisting of a planar carbohydrate surface, a flow system with flow cell and a cuvette connected with a signal transducer.

56. The immobilized carbohydrate derivative biosensor according to claim 17, wherein the biosensor surface is a member selected from the group consisting of a gold surface, a modified gold surface, a plastic surface which has been modified with a gold surface, a silver

surface and a metallic surface.

57. The immobilized carbohydrate derivative biosensor according to claim 56, wherein the surface is modified with a polymer which chemically couples a carbohydrate.

58. The immobilized carbohydrate derivative biosensor according to claim 17, wherein the surface comprises silica coated with a gold layer.

59. The immobilized carbohydrate derivative biosensor according to claim 58, wherein the silica surface coated with a gold layer is modified with mercaptopropionic acid by dipping the surface in a 5 mM solution of the acid.

60. The immobilized carbohydrate derivative biosensor according to claim 59, wherein the carboxyl groups are thereafter modified with carbodiimide (EDC), whereafter Galα1-4Galβ-OEtSEtCONHNH$_2$ is coupled to the surface for 12 hours at pH 8.5, and the surface rinsed with a buffer.

61. A method of using the immobilized carbohydrate derivative biosensor according to claim 60, comprising:

dipping the surface in a sample containing bacteria of the urinary tract having Galα1-4Gal-specific receptor protein;

thereafter rinsing the surface with distilled water; and

determining the extent of binding of the bacteria to the surface.

62. The immobilized carbohydrate derivative biosensor according to claim 17, wherein the carbohydrate derivative comprises Galα1-4GalβOCH$_2$CH$_2$SCH$_2$CH$_2$C(O)-NHNH-BSA, wherein BSA is bovine serum albumin.

63. The immobilized carbohydrate derivative biosensor according to claim 17, wherein the carbohydrate derivative comprises Galα1-4Galβ-BSA, wherein BSA is bovine serum albumin.

64. The immobilized carbohydrate derivative biosensor according to claim 17, wherein said surface comprises a means for monitoring a physical signal.

65. The biosensor according to claim 64, wherein said means for monitoring a physical signal is at least one member selected from the group consisting of a photometer, a chemical electrode, an electrochemical electrode, a temperature signal transducer, and a pressure signal transducer.

66. A method of using the biosensor according to claim 17 to determine the presence or amount of a biomolecule, comprising the steps of:

exposing the biosensor to a sample containing a biomolecule to be measured;

binding the biomolecule; and

measuring the presence or amount of the biomolecule.

67. A measuring device for measuring optical reflectance in air, comprising the immobilized carbohydrate derivative biosensor according to claim 17, wherein the surface comprises a planar carbohydrate sensor.

68. The measuring device according to claim 67, wherein the planar carbohydrate sensor is in the form of a dipstick.

69. A configuration for measuring a presence or an amount of a biomolecule, comprising the immobilized carbohydrate derivative biosensor according to claim 17.--

REMARKS

Applicants respectfully requests entry of the newly-submitted claims prior to examination on the merits in this continuation application.

Claims 17-69 are pending in this application, as presented herein. Applicants respectfully submit that the newly submitted claims contain no new matter.

Support for the newly submitted claims of the application is to be found as in the following table:

Claim:	**Support:**
17	Original claim 1, and page 3, lines 2-3.
18	Page 3, lines 4-10.
19	Page 3, lines 4-10
20	Page 3, lines 4-10.
21	Page 3, lines 4-10.
22	Page 3, lines 11-19.
23	Page 3, lines 11-19.
24	Page 3, lines 11-19.
25	Page 3, lines 11-19.
26	Page 3, lines 11-19.
27	Page 3, lines 11-19.
28	Page 3, lines 11-19.
29	Page 3, lines 11-19.
30	Page 3, lines 11-19.
31	Original claim 1; page 1, lines 1-3.
32	Page 3, lines 20-24.
33	Page 3, line 25 to page 4, line 5.
34	Page 4, lines 6-12.
35	Page 4, lines 6-12.
36	Page 4, lines 13-25.
37	Page 4, lines 13-25.

38	Page 4, lines 13-25.
39	Page 4, lines 26-30.
40	Page 4, line 31 to page 5, line 9.
41	Page 4, line 31 to page 5, line 9.
42	Page 4, line 31 to page 5, line 9.
43	Page 4, line 31 to page 5, line 9.
44	Page 5, lines 12-16.
45	Page 5, lines 12-16.
46	Page 5, lines 12-16.
47	Page 5, lines 17-29.
48	Page 5, line 30 to page 6, line 11.
49	Page 5, line 30 to page 6, line 11.
50	Page 5, line 30 to page 6, line 11.
51	Page 5, line 30 to page 6, line 11.
52	Page 5, line 30 to page 6, line 11.
53	Page 5, line 30 to page 6, line 11.
54	Page 5, line 30 to page 6, line 11.
55	Page 6, lines 12-27.
56	Page 7, lines 6-9.
57	Page 7, lines 6-9.
58	Page 7, line 14 to page 8, line 1.
59	Page 7, line 14 to page 8, line 1.
60	Page 7, line 14 to page 8, line 1.
61	Page 7, line 14 to page 8, line 1.

62	Page 8, lines 5-10.
63	Page 8, lines 5-10.
64	Page 1, lines 5-14.
65	Page 1, line 21 to page 2, line 26.
66	Page 7, line 14 to page 8, line 1.
67	Page 6, lines 12-27.
68	Page 6, lines 12-27.
69	Page 6, lines 12-27.

Examination on the merits is respectfully awaited.

If any additional fees are due in connection with the filing of this Amendment, such as additional fees under 37 C.F.R. §§ 1.16 or 1.17, please charge the fees to our Deposit Account No. 02-4300. If an additional extension of time under 37 C.F.R. § 1.136 is necessary and not accounted for in the papers filed herewith, such an extension is requested. The extension fee should also be charged to Deposit Account No. 02-4300. Similarly, any credit due should be credited to Deposit Account No. 02-4300.

Respectfully submitted,

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